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ORIGINAL ARTICLE

Impact of high dose versus low dose atorvastatin on contrast induced nephropathy in diabetic patients with acute coronary syndrome undergoing early percutaneous coronary intervention

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KEYWORDS

Atorvastatin;
Contrast induced nephropathy;
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Abstract *Background:* Statins with its anti-inflammatory and pleiotropic effects may prevent contrast induced nephropathy in high risk diabetic patients.
Aim of work: To compare between the effects of high and low dose atorvastatin on preventing contrast induced nephropathy after early coronary intervention in diabetic patients with acute coronary syndrome.
Patients and methods: The study included 80 consecutive diabetic patients presented with acute coronary syndrome and with normal renal function or with mild renal impairment (creatinine clearance 60–90 ml/min) who underwent early percutaneous coronary intervention. Patients were randomly assigned to one of two groups, Group (A) 40 patients who received 80 mg atorvastatin 12 h and 40 mg just before PCI. Group (B) 40 patients who received 10 mg atorvastatin at the same time points. Samples were taken for serum creatinine and creatinine clearance before, at 12 h and at 72 h after PCI. Multivariable regression analysis did not identify any independent predictor of CIN.
Results: There were 5 cases of CIN in group A (12.5%) versus 7 in group B (17.5%), ($p > 0.05$). The incidence of post-PCI contrast-induced nephropathy was not significantly different between the study groups ($p > 0.05$). Univariate regression analysis identified baseline blood urea ($p = 0.012$), blood urea after 12 h ($p = 0.030$), and blood urea after 72 h ($p = 0.003$) as predictors of CIN.

Abbreviations: CIN, contrast induced nehropathy; Cr, creatinine; CrCl, creatinine clearance; ACS, acute coronary syndrome; UA, unstable angina; NSTEMI, non ST-elevation myocardial infarction; IHD, ischemic heart disease; NIDDM, non-insulin dependent diabetes mellitus

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Conclusion: No significant difference between high and low doses of atorvastatin in preventing CIN in diabetic patients with normal or mild renal impairment presenting with acute coronary syndrome who underwent early PCI.

1. Introduction

Contrast-induced nephropathy (CIN) is an important potential complication of percutaneous coronary intervention (PCI). It occurs in approximately 7% of patients undergoing cardiac procedures currently.[1]

Although the incidence of CIN has decreased due to improved contrast media and better risk prevention measures in the past decade, there are continued substantial increases in CIN cases because of the increasing numbers of patients undergoing PCI.[2]

CIN generally resolves spontaneously in most instances, but patients may have prolonged hospital stay, increased risk of in-hospital death and higher long-term mortality rates.[3] There has been considerable interest in searching for effective strategies to prevent CIN.

Beside peri-procedural hydration, pharmacological prophylactic strategies have received considerable attention in recent years.[4] However, the pathophysiology of CIN is not well known. Some studies have suggested that oxidative stress, inflammation, reduction in renal blood flow and direct tubular cell damage by contrast media might play important roles in the organ injury process.[5]

Statins inhibit (hepatic 3-hydroxy-3-methylglutaryl coenzyme A reductase) with consequent suppression of cholesterol biosynthesis. The advent of these drugs has greatly impacted the treatment of cardiovascular disease.[6] In addition, several clinical and basic science investigations have demonstrated these statins may provide beneficial effects outside of reductions in low-density lipoproteins (LDL) and triglycerides (TG).[7]

Statins exert a number of protective effects involving the improvement of endothelial function, stabilization of atherosclerotic plaque, decrease of oxidative stress and inflammation, and inhibition of thrombogenic response[8]: the so-called pleiotropic effects. Their benefit has also been largely demonstrated in the setting of PCI by the prevention of peri-procedural myocardial and renal damage.

2. Aim of the work

To compare between the effect of high-dose and low dose atorvastatin on preventing contrast induced nephropathy after early percutaneous coronary intervention in diabetic patients with acute coronary syndrome.

2.1. Methods

2.1.1. Study population

The study included 80 consecutive diabetic patients with NIDDM with normal kidney function or mild renal impairment (pre-procedural serum creatinine level $\geqslant$1.5 mg/dl or creatinine clearance between 60 and 90 ml/min) with acute coronary syndrome (NSTE-ACS) who underwent PCI within 48 h of symptom onset.

2.1.2. Patients were randomly assigned to one of two groups

Group (A) [40 patients] received 80 mg atorvastatin 12 h and 40 mg just before PCI. **Group (B)** [40 patients] received 10 mg atorvastatin at the same time points.

The design was single-blinded randomized controlled trial. Investigators were aware of allocation group, while patients were blinded. The method of randomization was consecutive repetition, for example (patient 1 in group A, 2 in group B, 3 in group A, etc.).

The following patients were excluded from the study: ST elevation myocardial infarction (STEMI), contra indication to statins, liver impairment, exceeding maximum allowance of contrast dose calculated as (4 × creatinine clearance) or (body weight (kilograms) × 5 ml/serum creatinine), moderate to severe renal impairment (serum creatinine $\geqslant$3 mg/dl or creatinine clearance $\leqslant$60 ml/min), and previous use of other statins.

2.1.3. Procedures

All patients were admitted in coronary care unit for monitoring and investigations and received medications (Acetyl salicylic acid, clopidogrel, anticoagulation, beta blockers and angiotensin converting enzyme inhibitors, etc. according to each case separately. All patients received atorvastatin 10 mg/day from the day of admission.

All patients were subjected to thorough history taking together with full clinical examination including general and local cardiac examination was done.

The following investigations were done for all patients: (1) ***12 lead ECG.*** (2) ***Biomarkers:*** serial cardiac biomarkers (creatine phosphokinase (CK), CKMB and troponin) on admission and every 12 h. (3) ***Complete blood count, HbA1c*** (*for diabetic control*), ***lipid profile*** (Serum Cholesterol, Triglycerides level, HDL Cholesterol level and LDL Cholesterol level), liver function tests (SGOT–SGPT). (4) ***Serum creatinine and creatinine clearance (CrCl)***: by study design blood samples were drawn before and at 12 and 72 h after PCI for measurement of serum creatinine and the post-procedure peak value was used. Creatinine clearance (CrCl) was calculated by the Cockcroft–Gault formula: CrCl = ([140 − age] × weight/serum creatinine × 72) with adjustment for female gender (CrCl female = CrCl × 0.85).[9] Patients with pre-existing renal impairment received intravenous hydration with normal saline at 1 ml/h/kg body weight for $\geqslant$12 h before and $\geqslant$24 h after intervention.

Coronary angiography was done within 48 h of symptoms.

Clopidogrel preparation before PCI: patients who were not receiving regular clopidogrel (75 mg daily) before the procedure they were given 300–600 mg clopidogrel 4–8 h before PCI.[10]